

CLAIMS

1. An *in vitro* method of determining whether or not an individual has metastasized colorectal cancer cells comprising the steps of examining a sample of
5 extraintestinal tissue and/or body fluids from an individual to determine whether CRCA-1 transcript is being expressed by cells in said sample wherein expression of said CRCA-1 transcript is indicative of the presence of metastasized colorectal cancer cells in said sample.
- 10 2. The method of claim 1 wherein expression of said CRCA-1 transcript by said cells is determined by immunoassay wherein said sample is contacted with detectable antibodies that specifically bind to a CRCA-1 translation product.
3. The method of claim 1 wherein expression of said
15 CRCA-1 transcript by said cells is determined by polymerase chain reaction wherein said sample is contacted with primers that selectively amplify said CRCA-1 transcript or cDNA generated therefrom.
4. An *in vitro* method of determining whether or not a
20 tumor cell is a colorectal tumor cell comprising the steps of determining whether said tumor cell expresses CRCA-1 transcript wherein expression of CRCA-1 transcript indicates that the tumor cell is a colorectal tumor cell.
5. The method of claim 4 wherein expression of said
25 CRCA-1 transcript by said tumor cells is determined by immunoassay wherein said cell is contacted with detectable antibodies that specifically bind to a CRCA-1 translation product.
6. The method of claim 4 wherein expression of said
30 CRCA-1 transcript by said tumor cells is determined by polymerase chain reaction wherein said cell is contacted

with primers that selectively amplify said CRCA-1 transcript or cDNA generated therefrom.

7. An *in vitro* method of determining whether or not an individual has metastasized colorectal cancer comprising the steps of examining a sample of extraintestinal tissue and/or body fluids from an individual to determine whether a CRCA-1 translation product is present in said sample, wherein the presence of a CRCA-1 translation product in said sample indicates that said individual has metastasized colorectal cancer.

8. The method of claim 7 wherein said CRCA-1 translation product is detected by immunoassay wherein said sample is contacted with detectable antibodies that specifically bind to a CRCA-1 translation product.

9. The method of claim 8 wherein said sample is body fluid.

10. The method of claim 9 wherein said sample is blood.

11. An *in vitro* method of determining whether or not an individual has metastasized colorectal cancer comprising the steps of examining a sample of extraintestinal tissue and/or body fluids from an individual to determine whether a CRCA-1 transcript is present in said sample, wherein the presence of a CRCA-1 translation product in said sample indicates that said individual has metastasized colorectal cancer.

12. The method of claim 11 wherein said CRCA-1 transcript is detected by polymerase chain reaction assay using primers which specifically amplify CRCA-1 transcript sequences.

13. An *in vitro* assay kit for determining whether or not an individual has metastasized colorectal cancer by detecting the presence of a CRCA-1 translation product in a sample of extraintestinal tissue and/or body fluids from an individual, the presence of CRCA-1 translation product is present in said sample, wherein the presence of CRCA-1 translation product in said sample indicates that individual has metastasized colorectal cancer, said kit comprising:

 a container comprising antibodies specific for a CRCA-1 translation product;
 instruction for using said kit.

14. The kit of claim 13 further comprising a container that comprises a positive control; wherein said positive control is a sample containing a CRCA-1 translation product that binds to said antibodies.

15. The kit of claim 13 further comprising a container that comprises negative control; wherein said negative control is a sample free of said CRCA-1 translation product.

16. The kit of claim 13 further comprising a container that comprises a detectable antibody that binds to said antibodies specific for said CRCA-1 translation product.

17. An *in vitro* PCR assay kit for determining whether or not an individual has colorectal cancer by detecting the presence of CRCA-1 transcript in a sample of extraintestinal tissue and/or body fluids from an individual, wherein the presence of said CRCA-1 transcript in said sample indicates that individual has colorectal cancer, said kit comprising:

 a first container comprising PCR primers that specifically amplify said CRCA-1 transcript or cDNA generated therefrom;

 a second container comprising a size marker, said size marker being the expected size of amplified DNA if said CRCA-1 transcript is present in said sample; and

instructions for using said kit.

18. A substantially pure protein having an amino acid sequence selected from the group consisting of SEQ ID NO:2-81 and functional fragments thereof.

5 19. The protein of claim 18 wherein said protein has an amino acid sequence selected from the group consisting of SEQ ID NO:2-81.

20. An isolated antibody which binds to an epitope on a protein of claim 19.

10 21. The antibody of claim 20 wherein said antibody is a monoclonal antibody.

22. An isolated nucleic acid molecule that comprises a nucleic acid sequence that encodes a protein of claim 18.

23. The nucleic acid molecule of claim 22 wherein said
15 protein encoded by said nucleic acid sequence has an amino acid sequence selected from the group consisting of SEQ ID NO:2-81.

24. A recombinant expression vector comprising the nucleic acid molecule of claim 23.

20 25. A host cell comprising the recombinant expression vector of claim 24.

26. An isolated nucleic acid molecule having a nucleic acid sequence of SEQ ID NO:1 or a functional fragment thereof.

25 27. The nucleic acid molecule of claim 26 having a nucleic acid sequence of SEQ ID NO:1.

28. A recombinant expression vector comprising the nucleic acid molecule of claim 27.
29. A host cell comprising the recombinant expression vector of claim 28.
- 5 30. The nucleic acid molecule of claim 26 consisting of a functional fragment of SEQ ID NO:1 having at least 10 nucleotides.
31. The nucleic acid molecule of claim 26 consisting of a functional fragment of SEQ ID NO:1 having 12-150
10 nucleotides.
32. The nucleic acid molecule of claim 26 consisting of a functional fragment of SEQ ID NO:1 having 15-50 nucleotides.
33. An oligonucleotide molecule comprising a
15 nucleotide sequence complimentary to a functional fragment of SEQ ID NO:1 having nucleotide sequence of at least 5 nucleotides.
34. The oligonucleotide molecule of claim 33 comprising a nucleotide sequence complimentary to a
20 functional fragment of SEQ ID NO:1 having nucleotide sequence of 5-50 nucleotides.
35. The oligonucleotide molecule of claim 33 comprising a nucleotide sequence complimentary to a functional fragment of SEQ ID NO:1 having nucleotide
25 sequence of 10-40 nucleotides.
36. The oligonucleotide molecule of claim 33 comprising a nucleotide sequence complimentary to a functional fragment of SEQ ID NO:1 having nucleotide sequence of 15-25 nucleotides.

37. The oligonucleotide molecule of claim 33 comprising a nucleotide sequence complimentary to a functional fragment of SEQ ID NO:1 having nucleotide sequence of 10-150 nucleotides.
- 5 38. The oligonucleotide molecule of claim 33 comprising a nucleotide sequence complimentary to a functional fragment of SEQ ID NO:1 having nucleotide sequence of 18-28 nucleotides.
39. A conjugated compound comprising:
- 10 a) a CRCA-1 translation product binding moiety; and,
- b) an active moiety.
40. The compound of claim 39 wherein said active moiety is a radiostable active agent.
- 15 41. The compound of claim 39 wherein said active moiety is radioactive.
42. The compound of claim 39 wherein said an active moiety is a therapeutic agent.
43. The compound of claim 39 wherein said an active
20 moiety is an imaging agent.
44. The compound of claim 39 wherein said an active moiety is an antisense compound.
45. The compound of claim 39 wherein said an active moiety is selected from the group consisting of:
- 25 methotrexate, doxorubicin, daunorubicin, cytosinarabioside, etoposide, 5-4 fluorouracil, melphalan, chlorambucil, cis-platinum, vindesine, mitomycin, bleomycin, purothionin, macromomycin, 1,4-benzoquinone derivatives, trenimon, ricin, ricin A chain, *Pseudomonas* exotoxin, diphtheria toxin,

Clostridium perfringens phospholipase C, bovine pancreatic ribonuclease, pokeweed antiviral protein, abrin, abrin A chain, cobra venom factor, gelonin, saporin, modeccin, viscumin, volkensin, alkaline phosphatase, nitroimidazole, 5 metronidazole, misonidazole, ⁴⁷Sc, ⁶⁷Cu, ⁹⁰Y, ¹⁰⁹Pd, ¹²³I, ¹²⁵I, ¹³¹I, ¹⁸⁶Re, ¹⁸⁸Re, ¹⁹⁹Au, ²¹¹At, ²¹²Pb, ²¹²B, ³²P and ³³P, ⁷¹Ge, ⁷⁷As, ¹⁰³Pb, ¹⁰⁵Rh, ¹¹¹Ag, ¹¹⁹Sb, ¹²¹Sn, ¹³¹Cs, ¹⁴³Pr, ¹⁶¹Tb, ¹⁷⁷Lu, ¹⁹¹Os, ^{193M}Pt, ¹⁹⁷Hg, ⁴³K, ⁵²Fe, ⁵⁷Co, ⁶⁷Cu, ⁶⁷Ga, ⁶⁸Ga, ⁷⁷Br, ⁸¹Rb/^{81M}Kr, ^{87M}Sr, ^{99M}Tc, ¹¹¹In, ^{113M}In, ¹²³I, ¹²⁵I, ¹²⁷Cs, ¹²⁹Cs, ¹³¹I, ¹³²I, ¹⁹⁷Hg, 10 ²⁰³Pb and ²⁰⁶Bi.

46. The compound of claim 39 wherein said an active moiety is an antisense molecule that hybridizes to nucleotide sequences of DNA or RNA that encode a gene selected from the group consisting of: hereditary 15 nonpolyposis coli (HNPCC) genes such as hMSH2, hMLH1, hPMS1, and hPMS2, Ras, adenomatous polyposis coli (APC), ERBB-1/HER-1, ERBB-2/HER-2, p53 Tumor Suppressor, MYB, FOS, ABL, MYC, Protein Tyrosine Phosphatase G1, Cyclic AMP-Dependent Protein Kinase (PKA), CRIPTO, Transforming Growth Factor 20 Alpha and 1p.

47. A pharmaceutical composition comprising:
a) a pharmaceutically acceptable carrier or diluent, and,
25 b) a compound according to claim 39.

48. A method of treating an individual suspected of suffering from metastasized colorectal cancer comprising the steps of administering to said individual a pharmaceutical composition according to claim 47 wherein said active moiety 30 is a therapeutic agent, said composition is administered in an amount effective for therapeutic use in a humans suffering from colorectal cancer.

49. A method of radioimaging metastasized colorectal cancer cells comprising the steps of administering to an

individual a pharmaceutical composition according to claim 47 wherein said active moiety is an imaging agent, said composition is administered in an amount effective for diagnostic use in a humans suffering from colorectal cancer.

5 50. A method of treating an individual suspected of suffering from colorectal cancer or of preventing colorectal cancer in an individual suspected of being susceptible to colorectal cancer comprising the steps of administering to said individual a therapeutically or prophylactically
10 effective amount of a pharmaceutical composition according to claim 47, wherein said active moiety is an antisense molecule that hybridizes to nucleotide sequences of DNA or RNA that encode a gene selected from the group consisting ... of: hereditary nonpolyposis coli (HNPCC) genes such as
15 hMSH2, hMLH1, hPMS1, and hPMS2, Ras, adenomatous polyposis coli (APC), ERBB-1/HER-1, ERBB-2/HER-2, p53 Tumor Suppressor, MYB, FOS, ABL, MYC, Protein Tyrosine Phosphatase G1, Cyclic AMP-Dependent Protein Kinase (PKA), CRIPTO, Transforming Growth Factor Alpha and 1p.

20 51. The method of claim 50 wherein said pharmaceutical composition is administered orally.

52. A method of delivery a nucleic acid molecule to intestinal tract cells of an individual comprising the steps of administering to said individual a pharmaceutical
25 composition comprising:

- a) a pharmaceutically acceptable carrier or diluent, and,
- b) a composition comprising:
 - i) a CRCA-1 translation product ligand;
 - 30 and,
 - ii) a nucleic acid molecule.

53. A vaccine composition comprising:

-- a) a protein comprising at least one epitope of a CRCA-1 translation product or a nucleic acid molecule that encodes said CRCA-1 translation product; and

b) a pharmaceutically acceptable carrier or
5 diluent..

54. A method of treating an individual who has metastasized colorectal cancer comprising the step of administering to such an individual a therapeutically effective amount of a vaccine composition of claim 53.

10 55. A method of treating an individual who has been identified as being susceptible to metastasized colorectal cancer comprising the step of administering to such an individual a prophylactically effective amount of a vaccine composition of claim 53.